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Anh Nguyen
05/04/04 11:46 AM

To: NCIC HPV@EPA
cc:
Subject: Fw: Environmental Defense comments on 1,3-Diphenylguanidine (CAS# 102-06-7)

----- Forwarded by Anh Nguyen/DC/USEPA/US on 05/04/2004 11:46 AM -----

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05/04/2004 09:38 AM

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cc: lucierg@msn.com, kflorini@environmentaldefense.org, rdenison@environmentaldefense.org
Subject: Environmental Defense comments on 1,3-Diphenylguanidine (CAS# 102-06-7)

(Submitted via Internet 5/4/04 to oppt.ncic@epa.gov, hpv.chemrtk@epa.gov, boswell.karen@epa.gov, chem.rtk@epa.gov, lucierg@msn.com and anne_lehuray@americanchemistry.com)

Environmental Defense appreciates this opportunity to submit comments on the robust summary/test plan for 1,3-Diphenylguanidine (CAS# 102-06-7).

This submission for 1,3-diphenylguanidine (DPG) was made by the American Chemistry Council. The submission is comprised of the final SIDS documents for this chemical that were reviewed and approved in April 2002 under the HPV program administered by the Organization for Economic Cooperation and Development (OECD).

The submission does appear to contain the SIDS elements required under the U.S. HPV program, and hence appears to fulfill U.S. program requirements. Nonetheless, we offer these additional comments based on our review.

This submission presents pseudo risk assessments by attempting to consistently downplay positive results of toxicology studies without adequate scientific justification. The SIAM submission does, however, include some exposure assessment information for workers, consumers and the general environment.
DPG is used as a primary accelerator in the vulcanization of rubber, as secondary accelerator for sulfur-containing compounds such as thiazoles and thiurams and for standardizing acids. Some releases to the environment occur from abrasion of tires and other rubber products, but this is not well-characterized. The OECD concluded that this chemical is a candidate for further work, specifically additional studies to obtain better information on the magnitude of environmental contamination arising from the various uses of rubber products containing DPG.

We are also concerned with the misleading risk assessment comments contained in the submission. For example, the documents repeatedly state that any observed toxic effects are a consequence of poor palatability of food containing DPG. These effects include neurotoxicity, hematologic effects and liver toxicity which are unlikely to be caused by bad tasting food.

Other specific comments are as follows:

1. DPG is toxic to fish, aquatic invertebrates and algae, so the OECD's recommendation to conduct additional studies on environmental releases and persistence should provide useful information.

2. Well-conducted rodent pharmacokinetic studies indicate that DPG is rapidly metabolized and cleared, so this substance should not accumulate in the human body.

3. DPG was evaluated for repeat dose toxicity by a number of studies, including NTP studies in rats and mice that indicate a NOEL of about 25 mg/kg based on a number of toxic endpoints.

4. DPG has also been evaluated in several reproductive and developmental toxicity studies, which indicate that it has some reproductive effects in both males and females. The documents attempt to discount the positive studies, but the justifications are far from convincing. This is particularly evident for changes in sperm motility and uterine weights. We also note that the test plan indicates a NOEL of 5 mg/kg in pregnant rats, which is a level 5-10 times lower than the NOEL derived from the repeat dose studies. Unanswered questions include: What toxic endpoint is used to obtain the NOEL in pregnant rats, and why are pregnant rats more sensitive to DPG than non-pregnant rats?

5. A number of genetic toxicity tests indicate that DPG has weak or no genotoxicity.

Thank you for this opportunity to comment.

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